

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 10/517,518
Applicant : Stefan SPERL
Filed : July 1, 2005
TC/A.U. : 1621
Examiner : S. KUMAR

Docket No. : 2923-671
Customer No. : 06449
Confirmation No. : 1246

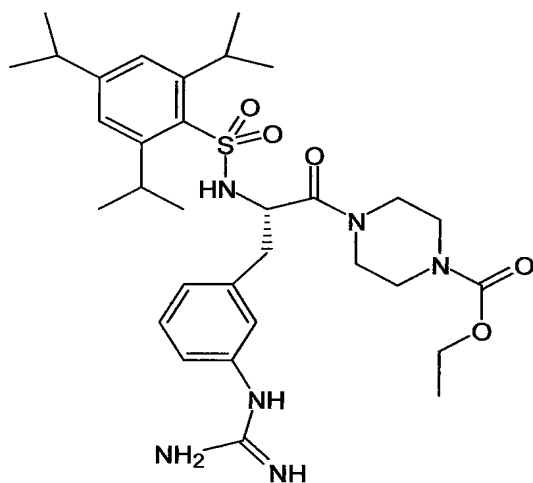
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION UNDER 37 C.F.R. '1.132

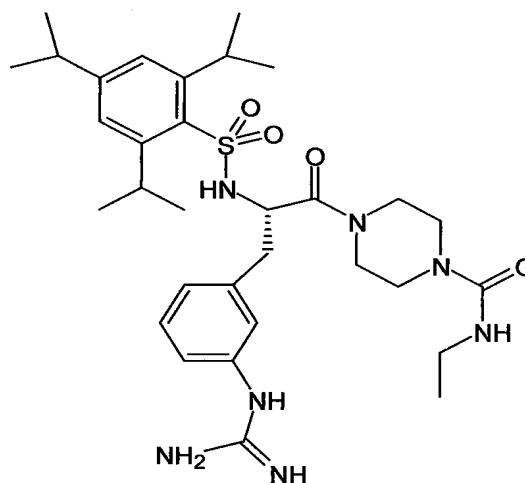
I, Stefan Sperl, declare as follows:

1. I am the inventor of the above-identified application.
2. My educational background is as follows: Chemist, PhD. I am currently employed as a Project Manager Preclinics at Nabriva Therapeutics GmbH, Vienna, Austria.
3. The following experiments were conducted by me or under my supervision and control.
4. The in-vitro inhibition of urokinase, plasmin and thrombin by two compounds were determined as set forth in Examples 3 and 4 of the present application. The data are presented below.

Compound	K _i , uPA [μ M]	K _i , plasmin [μ M]	K _i ,thrombin [μ M]
WX-682	0.47	3.8	12.3
WX-684	0.9	4	>25



WX-682



WX-684

I note that Compound WX-682 is the subject of Example 4 of the present application. Those data show that the compounds have a much higher selectivity for urokinase compared to thrombin and plasmin.

5. I am also aware of data presented in the Pentapharm Product Catalog 1998 with respect to the inhibition of various serine proteinases by a number of amidino phenylalanine compounds; relevant pages are attached hereto. The compound identified as Pefabloc® uPA is analogous to compound WX-682, except that it contains a 3-amidino group instead of a 3-guanidino group. According to page 25 of the catalog, the 3-amidino compound had the

following inhibition constants: uPA: 0.41 μ M; plasmin: 1.0 μ M; and thrombin: 0.67 μ M. It is evident that the 3-amidino compound was much less selective for urokinase compared to thrombin and plasmin, than is the corresponding 3-guanidino compound WX-682. The other amidino phenylalanine compounds in the catalog likewise failed to show specificity for urokinase (see data for Pefabloc® TH, TH1158, PL, Xa, Tryp and Try1420 products on page 25). Thus, the high selectivity of the guanidine compounds is surprising and unexpected.

6. All statements made herein of my own knowledge are true, and all statements made on information and belief are believed to be true. All statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Stefan Spert
Name

25/07/2007
Date

#1412682